[0031] FIG. 7 presents an exemplary timing sequence for operation of the ion funnel trap that includes a gate cycle that provides for accumulation, storage, and ejection of ions in the ion funnel trap. The timing sequence is shown for an instrument configuration that includes the ion funnel trap coupled to an electrodynamic ion funnel (preceding stage) and a dual-stage reflectron oa-time-of-flight mass spectrometer (subsequent stage). The instrument configuration is not limited. In an alternate configuration, an ion-mobility-quadrupole-time-of-flight mass spectrometer (IMS TOF-MS) as a (subsequent stage) was used. The TOF-MS is detailed, e.g., by Clowers et al. (Analytical Chemistry, 2008, 80, pgs. 612-623) incorporated herein. Here, an electrospray ionization source provides ions through the ion funnel to the IFT. A key aspect of IFT performance is the configuration of the trapping portion. At lower pressure (e.g., 1 Torr), the ion trap can be configured with a single entrance grid and a single exit grid, e.g., as described by Ibrahim et al. (Analytical Chemistry, 2007, 79, 7845-7852). At higher pressure (e.g., 4 Torr), use of an additional trapping grid results in accelerated ion extraction from the trapping portion, e.g., as described by Clowers et al. (Analytical Chemistry, 2008, 80, pgs. 612-623), which reference is incorporated herein in its entirety. Lower and higher pressure configurations are referred to herein as two and three grid arrangements, respectively. Pulsing voltages applied to the entrance grid and the exit grid control ion populations introduced into the trap, as well as to control ion storage and extraction times, respectively. During the accumulation and storage events, electric field gradient within the inlet portion (FIG. 1a) is, e.g., ~1 V/cm. This field is a combination of dc-voltage applied to the ion funnel and field penetration of dc-only grids that surround the trapping portion of the IFT. When ejecting ions from the IFT, electric field gradient within the 5 mm immediately preceding the dc-only trapping grid is, e.g., ~19 V/cm. Number of ions accumulated in the ion funnel trap increases proportionally to the accumulation time. The dc-gradient in the trapping portion can be varied independently from the coupled ion funnel by adjusting potentials of the first and last electrodes in the trapping portion. Ions passing through trapping portion are recollimated in the converging geometry of the outlet portion and are then focused into a subsequent stage. FIG. 7 shows that one IMS experiment encompassing ion accumulation, storage, and ejection events occurs on the time scale of multiple (e.g., 600) TOF-MS spectra acquisitions. Here, ion trap events are synchronous with TOF trigger pulses. TOF-MS generates a sequence of trigger pulses whose repetition rate and number determines the trapping and acquisition times, respectively. Transistor-Transistor Logic (TTL) (output) signals from the TOF are fed into three independent high-voltage switches that provide pulsed voltages to the entrance grid, and the trapping and exit grids (e.g., as pulsing grids). To enable ion injection and accumulation events, potentials at the trapping and exit grids (or just the exit grid for a two grid arrangement) are raised to a level that provides efficient ion beam blocking (see FIG. 6). Ion storage is accomplished by increasing the potential at the entrance grid to a level that ensures blocking of the incoming ion beam at the entrance grid, while trapping and exit grid potentials (or exit grid potential for the two grid arrangement) remain unchanged. The ion extraction event is characterized by reduction in the trapping and exit grid potentials (or just the exit grid potential for the two grid arrangement) to a level

corresponding to an optimum ion transmission. In an alternate mode, neither grid is pulsed so ions enter and traverse the IFT continuously.

[0032] FIG. 8 is a plot showing ion current measured at the collisional quadrupole rods obtained from ESI of a 1 μM Reserpine solution. Ion current pulses were acquired at different accumulation times in the ion trap. The current pulses generated by ions accumulated in the trap are two orders of magnitude higher than the total ion current of the continuous beam. Maximum amplitude of the ion current pulse (28 nA at 100 ms accumulation time) exceeded that of the continuous beam (216 pA) by more than 2 orders of magnitude. Area under each current pulse corresponds to the number of charges released.

[0033] FIG. 9 is a plot showing the trap capacity and efficiency of the ion trap. Charges released from the ion trap are calculated from areas under traces in FIG. 8. As shown in the figure, at present, the ion trap has a charge capacity of ~3×10^7 charges. Number of charges increases as the accumulation time increases. While the total number of charges reaches ~3×10^7, the linear range for the ion trap extends to only ~1×10^7 charges. Trapping efficiency is the ratio of the number of ions released from the trap (measured, e.g., at a collisional quadrupole) after a single accumulation event to the number of ions introduced into the trap over the same accumulation period. Number of ions introduced into the ion trap is calculated as a product of the continuous ion current and accumulation time. As shown in the figure, trap efficiency reaches 80% at shorter accumulation times (<10 ms) and decreases to from 20% to 30% (~25%) as the IFT reaches its charge capacity (for accumulation times >50 ms). Data indicate that lower dc-gradients give rise to more efficient ion accumulation while higher dc-gradients result in lower trapping efficiency. The drastic decrease in ion accumulation efficiency with an increase in the ion trap dc-field is related to axial compression of the ion cloud and associated space charge effects. Because of the cylindrical geometry of the trap, the dc-trapping field has a radial component that tends to eject ions in the radial direction where they experience higher rf-oscillations and are lost to the electrodes. When the axial electric field is sufficiently low (4 V/cm), the accumulated ion cloud extends axially, thus increasing the trap capacity and its efficiency. Transmission efficiency is determined as the ratio of the pulsed ion current (expressed as number of charges) at the charge collector to the pulsed ion current at the collisional quadrupole rods as a function of the number of charges exiting the ion trap. Pulsed ion current transmission decreases as the total number of ions transmitted through the collisional quadrupole increase. Improvements in the transmission of dense ion packets through the quadrupole interface are feasible with more efficient ion focusing at higher residual gas pressures. In proteomic. experiments, rigorous control over ion populations accumulated in the ion trap can be accomplished using automated gain control. Automated gain control capability is achieved by alternating operation of the ion funnel between continuous and trapping modes.

[0034] FIG. 10 is a mass spectrum for a 10 nM mixture of bradykinin (SEQ. ID. NO: 1) and fibrinopeptide-A (SEQ. ID. NO: 2) processed in trapping and continuous modes in a TOF-MS configuration that includes an IFT, according to an embodiment of the method of the invention. Mixture was prepared with 10 nM for each peptide in the mixture. Aliquots of the sample mixture were analyzed in the TOF mass spectrometer in both Trapping and Continuous modes. For the